

WELLCOME INSTITUTE LIBRARY	
Coll.	weITROmec
Call	pan
No.	WR 350
	1898
	B 730

ON SARE SORE

P.F.BOROVSKY

Trans.Royal Society of Tropical Medicine and Hygiene.

1898



22200059876

where he had spent 40 years of his working life, on December 16th, 1932, at the age of 69.

The accompanying portrait (Frontispiece), taken in 1895, represents BOROVSKY—wearing the uniform of a medical officer in the Imperial Russian Army—at the age of 32, at the period when his researches on oriental sore were being conducted. The original portrait was given to the late Prof. G. H. F. NUTTALL, F.R.S., by Prof. E. N. PAWLOWSKY, of the Military Medical Academy, Leningrad, for inclusion in the "Portrait Gallery" of parasitologists at the Molteno Institute, Cambridge, and has been kindly placed at my disposal by Prof. D. KEILIN, F.R.S. The biographical data for this note were compiled from articles by I. I. ORLOV (*Pensée Méd. Uzbequistane*, 2, 1927, p. 5), E. N. PAWLOWSKY (*Ibid.*, p. 16), L. ISSAEV (*Med. Parasitol. & Parasit. Dis.*, Moscow, 1, 1933, p. 277) and from two anonymous obituary notices (*Ibid.*, p. 287, and *Munch. med. Wschr.* 80, 1933, p. 518).

APPENDIX II.

ON SART SORE.¹

BY

P. F. BOROVSKY,

Junior House Surgeon, Bacteriological Department of the Tashkent Military Hospital.

p. 925

Sart sore is not widely distributed in Tashkent; it occurs only sporadically and new arrivals in the country do not invariably contract the disease as in the case of Pendeh sore, Aleppo boil, etc. The sores very rarely appear in the form of a multiple eruption; in most cases two or three sores occur, while solitary sores are not uncommon. Sart sore is thus more restricted in its distribution than Pendeh sore and its incidence amongst the troops is not of an epidemic character. Nevertheless, judging from the clinical and the anatomico-pathological pictures described by HEIDENREICH² and by RAPTSCHESKY, Sart sore is probably identical with Pendeh sore. It may therefore be assumed that the cause must be the same, though the conditions for the manifestation and spread of the infection are different. Moreover, in the Murgab valley itself the disease is not uniformly distributed, according to the investigations of RAPTSCHESKY (*Voenno-Medicinskij Zhurnal*, 1889, Book VIII). HEIDENREICH and RAPTSCHESKY differ in their conclusions both as regards the cause of Pendeh sore and the method of its dissemination.

p. 926

On perusing both investigations one is forced to conclude that HEIDENREICH has investigated unsuitable old cases which had already become ulcerated, and that consequently the results obtained were doubtful. Thus,

*¹[Published in: *Voenno-Medicinskij Zhurnal* (= *Military Medical Journal*), St. Petersburg, November, 1898, Part clxxxxv, Book 11 (76th year) pp. 925-941, 2 text-figs. (In Russian.)

Translated from the Russian text by C. A. HOARE.

The pagination of the original text is indicated in the margins; the annotations in italics between square brackets—both in the text and in the footnotes—are interpolated by the translator: those not distinguished in this way are found in the original.]

²[In some publications this name is spelt "Heydenreich."—C.A.H.]

HEIDENREICH³ says: "if the end of a platinum wire is introduced into the fluid issuing from a scab subjected to pressure, and if a stab is made with this infected wire into sterile [*nutrient gelatin*]⁴ in a sterile test-tube it is sometimes possible, after several days, to obtain a culture of a special micrococcus." In view of this statement one can understand the scepticism regarding the "micrococcus Biskra, DUCLAUX et HEIDENREICH," especially since RAPTSCHESKY has obtained different results in his investigation. On account of the controversy regarding the aetiology of "oriental sore," and with the object of ascertaining whether Sart sore is identical with Pendeh sore, we undertook at the end of 1894 a bacteriological and anatomico-pathological investigation. The material for the investigation was provided partly by hospital patients and partly by out-patients. Most of the cases selected were in the early period, *i.e.* in the non-ulcerating stage, the importance of which was rightly pointed out by RAPTSCHESKY.

The investigation was carried out with long intervals owing to lack of suitable material. Frequently several months would elapse before a single suitable case was encountered, and this was due not so much to the rareness of the disease as to the fact that patients in the first period of the disease pay little attention to it, since at the beginning it causes no discomfort, and therefore in most cases they apply for assistance only during the period of ulceration.

THE CLINICAL COURSE OF SART SORE.

In the initial phase of its development Sart sore appears in the form of a nodule elevated above the surface of the skin and perceptible both to the eye and to the touch. The nodule, which is of a dark red hue, passes imperceptibly into the healthy tissue of the skin. Palpation is not painful; the patient feels no discomfort, except a slight itching, and even this is not always experienced. After 10 to 20 days (we have not seen any earlier cases) there appears in the centre of the nodule a slight depression covered by a grayish, firmly adherent crust. On removal of this a small opening is revealed discharging a slightly turbid serous fluid. It is usually at this period that the nodules begin to ulcerate, starting from the centre, while an infiltration spreads into the surrounding healthy tissues. p. 927

When kept clean and in the absence of external irritation the nodule does not ulcerate, but begins to increase more or less regularly, sometimes assuming the appearance of a plaque about 4 to 5 cm. in diameter, while the skin takes on a bluish tint and its surface becomes considerably desquamated. Sometimes in the infiltrated area of the skin the papillae begin to proliferate and the surface becomes covered with numerous minute papillae. The papillae are more defined in the centre, diminishing towards the periphery, while at the edge the

³L. L. HEIDENREICH: Pendeh Sore (Tropical Sore). Attacks, cause, identification, etc. Publ. by Chief Milit. Med. Dept. [St. Petersburg, 1888. (Review in: *Ann. Inst. Pasteur*, 3, 1889, 445.)]

⁴[In the original only the initials, indicating "meat-gelatin," are given.—C.A.H.]

skin is smooth. The margins of the area of infiltration are slightly raised above the middle: between the papillae there is an accumulation of desquamating epithelium, and in some places there are small fissures discharging a slightly turbid fluid.

In Sart sore the infiltration is continuous and individual nodules are not palpable.

Large papules are, however, comparatively rare; in most cases after 2 to 3 weeks a superficial ulcer is produced with a slightly eroded edge; the discharge from the ulcer is not copious and a crust is, therefore, easily formed; around the ulcer the infiltration area assumes a bluish-red hue and has a doughy consistence on palpation. We have never had the opportunity of seeing the lymph nodes in the course of Sart sore; in general this symptom⁵ (which is, according to RAPTSCHESKY, a complication of the sore) does not occur in the Sart sore of Tashkent.

The rate at which Sart sore spreads varies in different parts of the body. If the disease appears on the nose, the eye-lids, or the face in general, the infiltration increases far more rapidly.

p. 928

We have not observed natural healing and therefore possess no data for judging how long the sore can last; we have, however, observed several sores of more than a year's duration which had to be treated before they healed.

As regards the situations in which the sores appear, our observations confirm those of previous observers, *viz.* that the sore mainly attacks the exposed parts. But whereas in our cases the sores occurred most frequently on the face, according to RAPTSCHESKY, HEIDENREICH and others, the shin and forearm were the parts most frequently affected, and the face only to a lesser degree.

As to the time of year when the incidence of the disease is highest, in Tashkent the greatest number of cases appear in January, February, March and April, and then in November and December, while there are considerably fewer cases during the summer months.

The incidence of the disease is higher among the lower classes of the population, though cases also occur among the well-to-do.

Sart sore heals with the formation of a superficial, slightly depressed, flat cicatrix; this is at first of a darker colour, but as time passes it becomes paler and remains whiter than the surrounding parts.

As regards the diagnosis, it is difficult to confuse the sore with anything else if its development is taken into consideration.

We realize that ordinary ulcers of the shin and those which frequently affect the nose might give rise to doubts. However, in the first case cleanliness and rest rapidly produce an amelioration leading to cicatrization of common ulcers, whereas Sart sore remains for weeks in the same state under similar conditions; moreover, if attention is given to the appearance of the area of

⁵[*Viz.*, enlargement of lymph nodes due to lymphangitis: cf. HEIDENREICH, 1888 (abstract in *Ann. Inst. Pasteur*, 3, 1889, p. 445).—C.A.H.]

infiltration—its doughy consistence, indolence, the bluish-red hue of the skin above the infiltration—its identification presents no difficulties. It is sufficient to see the sore once or twice to be able to diagnose it without error.

As regards the lesion on the nose, this may at first lead to confusion with lupus, but the doughy consistence and the more diffuse character of the infiltration in the case of Sart sore, the absence of minute nodules separated from the main focus by healthy patches of skin, are sufficient for the differentiation of these disorders, apart from the difference in the rate of spreading. As stated above, Sart sore spreads rapidly over the whole nose, whereas in lupus the process is much slower. In the later stage of development it is impossible to confuse the two diseases since lupus destroys the cartilage and bone, whereas Sart sore never penetrates beyond the skin.

p. 929

PATHOLOGICAL ANATOMY.

The earliest period at which we had occasion to examine a sore was after 2 weeks. The following are the changes observed: There are no special changes in the epidermal layer; the Malpighian epithelial layer is already slightly altered—in the centre of the papule the interpapillary projections of the Malpighian layer are shorter than at the periphery and in places the granulation tissue penetrates through them in the form of rounded rods. The chief changes, however, occur in the dermis. The dermal papillae are permeated with the granulation elements, mostly in the form of epithelioid cells; the proliferation of the granulation tissue proceeds mainly along the vessels. The accumulation of cells is greatest in the centre of the papule, resulting in the formation of an area of dense infiltration, while towards the periphery the islets of granulation tissue are separated from each other by areas of more or less modified connective tissue. In the deeper parts of the corium, where it passes into the subcutaneous connective tissue, are scattered accumulations of granulation elements in the form of isolated foci, which are also situated around the vessels. These deep accumulations of cells are separated from the more superficial ones by a thick layer of unaltered or slightly altered connective tissue. The blood-vessels are altered even at this early stage of development of the sore: the endothelium is swollen, inside the vessels there are accumulations of white corpuscles; the minute arteries and veins are not infrequently narrowed to the point of disappearance of the lumen, partly owing to the accumulation of lymphoid elements around them, and partly to changes in their walls.

In the papular stage the cellular infiltration is more marked in the reticular layer of the dermis than in the papillary layer. In the course of its further proliferation the granulation tissue approaches the surface, progressively disrupts and destroys the Malpighian epithelial layer, raises the epidermal layer and, having destroyed the latter at some point, spreads over the surface. For this reason it is not uncommon to encounter an entire strand of epidermis as well as of the Malpighian layer in the midst of the granulation tissue, whereas

p. 930

at the periphery, where there is less infiltration of the cellular elements, there can be observed a considerable thickening of the epithelial layer, the inter-papillary projections of the epithelium not infrequently branching and the boundary between the epithelium and the surrounding tissue not being sharply defined. This phenomenon has, however, long been noted in all kinds of chronic ulcerative processes of the skin. During the period of ulceration the changes in the vessels are more marked: the walls of the minute arteries and veins are infiltrated, the vessels in some parts being occluded. In the midst of the granulation tissue there occur free accumulations of red blood corpuscles, either still retaining their appearance or already having broken up and formed rounded or irregular yellow accumulations; such accumulations are scattered in different parts of the ulcer and also occur in the epithelial layer.

During the period of ulceration the granulation tissue undergoes further development in some parts and is transformed into connective tissue with a small number of spindle-shaped cells, this transition taking place in the more superficial layers, whereas from the deeper parts there develops a thick layer of granulation tissue.

AETIOLOGY.

The cause of Sart sore and of other similar (if not identical) "oriental sores," such as Pendeh sore, Aleppo boil, [*bouton de*] Biskra, the Elisabethpol "godovik"⁶ etc., has not been firmly established up to the present.

DUCLAUX, HEIDENREICH and CHANTEMESSE investigated the "*bouton de Biskra*" in 1884 and isolated in culture a micrococcus similar to (if not identical with) the golden staphylococcus [= *Staphylococcus aureus*].

p. 931

HEIDENREICH, who studied Pendeh sore in 1886, confirmed DUCLAUX's investigation, *viz.* he attributed the origin of the sore to the penetration into the skin of "micrococcus Biskra," which is apparently identical with the golden staphylococcus.

Dr. RAPTSCHESKY, who investigated Pendeh sore after HEIDENREICH, obtained different results: on examining the juice of the papules he isolated a streptococcus which differs from that of erysipelas and which he regards as the causative agent.

NICOLLE and NOURY-BEY have carried out a bacteriological investigation of Aleppo boil (*Annales de l'Institut Pasteur*, 1897, No. 9) and have also isolated a streptococcus which they regard as the causative agent. These authors studied nine cases: in three they obtained a pure culture of streptococcus, in five cases staphylococci developed together with the streptococci, and in one case bacilli were also present. Clinically Aleppo boil runs the same course as Sart sore and Pendeh sore: at the beginning there appears a papule of the size of an acne [*pustule*] which gradually increases in size; the papule is indolent and the

⁶[*godovik* = (*lit.*) annual: name for the Transcaucasian form of oriental sore, which usually persists for 1 year.—C.A.H.]

colour of the skin remains unchanged ; by the 3rd to the 5th month the papule becomes covered with a crust under which there is an ulcerated bleeding surface ; the pathological process extends further, there is an exudation of a sero-purulent fluid, and 3 to 4 months later cicatrization begins. According to NICOLLE and NOURY-BEY, the entire period of development of Aleppo boil is 11 to 12 months.

However, the species of streptococci isolated by RAPTSCHESKY and by NICOLLE and NOURY-BEY are different. RAPTSCHESKY's streptococcus is distinguished by slow growth : the colonies cultivated on agar-agar at the optimum temperature (30 to 36°) become visible to the naked eye only on the 3rd or 4th day in the form of small whitish discs. On gelatin their growth is still slower ; the streptococcus does not liquefy gelatin ; in stab cultures growth takes place only along the course of the stab, without any signs of growth over the surface. When grown in fluid nutritive media the streptococcus forms a fine white precipitate. The streptococcus isolated by NICOLLE and NOURY-BEY is characterized by rapid growth in all kinds of media : the development of the colony can be noticed even after 24 hours ; when growing in broth the streptococcus produces a golden-yellow colour.

From the foregoing it is obvious that there is a complete difference of opinion regarding the aetiology of "oriental sore." Before turning to the results of our own research, we shall give an account of the method of investigation. p. 932

If the patient was in hospital, the sore was dressed for several days with warm boric acid compresses ; then the papule was washed with alcohol and ether, after which it was excised and removed with instruments boiled in a solution of soda. A scraping was then immediately taken from its deep bleeding surface with a sterilized knife. By means of a platinum loop passed through a flame this scraping was transferred to gelatin or agar-agar which was poured out into Petri dishes ; or the superficial layers of the sore were removed with a sharp spoon, while with a second spoon scrapings were made from the deeper parts and were used for making smears on slides and for inoculation. The excised portions of the papules, and sometimes of the ulcers, intended for an anatomico-pathological investigation were first hardened in 95 per cent. alcohol and then embedded in celloidin for the preparation of sections. The very first cases studied by us produced unexpected results : streptococci were not obtained in cultures but in their stead there developed a small number of yellow and white staphylococcus colonies and sarcinae, the number of bacteria being so insignificant that in the second and third cultures only a few isolated colonies developed, in view of which we made only one culture in subsequent cases. Moreover, in smears from the juice of the papules microorganisms were either absent or only solitary cocci were encountered.

From the end of 1895 we began to examine the juice of papules and sores in which no inflammatory phenomena were manifested, in hanging drops, and were astonished by the presence of numerous motile corpuscles, some round,

some irregular, while some of them possessed pseudopodia.⁷ Since that time and up to the present we have found the same structures every time we have examined the juice and scrapings from the sores.

p. 933 The younger the papule the greater was the number of these corpuscles, whereas only a few of them were present in scrapings from the depth of the older sores. At the beginning, when we dried and fixed the smear directly over the flame, according to the method usually adopted, the examination of the smears gave negative results. Recently, however, when we proceeded to fix the smears with a mixture of absolute alcohol and ether, staining with Loeffler's solution revealed the same corpuscles which had been observed in the hanging drop. The size of these structures varies from $\frac{1}{2}\mu$ to 2μ , occasionally reaching 3μ , but in most cases their dimensions are from $1\frac{1}{2}\mu$ to 2μ . These corpuscles frequently have a fine process as long as, or sometimes longer than the diameter of the corpuscle; at the end of the process there is not infrequently a small globular thickening;⁸ sometimes several—two and three—of these processes are observed. The corpuscles described are colourless: they are sometimes homogeneous, or they appear to have a nucleus in the centre or at the periphery, while in some of them vacuoles can be seen.⁹ Moreover, in the hanging drop are observed minute dark structures of a round shape with one or several fine processes; the latter structures are very motile.¹⁰

The shape of the corpuscles is sometimes spherical and sometimes fusiform. Occasionally a change in their shape could be observed—an oval would change into a sphere, then into an irregularly-shaped body and afterwards again become oval.¹¹ In two cases spheres were observed measuring 4 to 5μ , having a double-contoured membrane and densely packed with round corpuscles. One such sphere was seen to be half empty, while in the other half the round corpuscles were also disposed outside the membrane.¹²

If a hanging drop preparation was left in a thermostat it showed considerable changes after 24 hours: the larger round bodies disappeared and broke up, while the number of the above-mentioned minute structures with fine processes increased.¹³ If the preparation was pure, all the structures disappeared after

⁷[It is possible that some of these "corpuscles" may have been blood platelets and that the motility refers to Brownian movement.—C.A.H.]

⁸[The appearance of the "corpuscles" described here would suggest that in some of the parasites only the nucleus and rod-shaped kinetoplast were visible, a not infrequent occurrence in poorly fixed tissues.—C.A.H.]

⁹[These cases probably refer to the whole parasite.—C.A.H.]

¹⁰[V. *supra*: footnote 7.]

¹¹[The apparent change of shape can be accounted for by the different views of the parasite, obtained in the course of its slow revolution.—C.A.H.]

¹²[These "spheres" represent detached fragments of the cytoplasm of the host-cells. They have been described by other authors, some of whom have regarded them as representing the parasite itself, while the true parasites were mistaken for its "spores" (CUNNINGHAM, 1885; FIRTH, 1891; and ROSS, 1903: the last in the case of kala-azar).—C.A.H.]

¹³[V. *supra*: footnote 7.]

2 or 3 days, whereas in the case of contamination with bacteria the latter, which were chiefly cocci, developed.

On examining sections of preparations fixed with 95 per cent. alcohol and stained, according to RAPTSCHEWSKY's directions, with Loeffler's solution we never found any streptococci, but there were masses of what at first appeared to be cocci, some round, but most of them oval, arranged in clumps which were frequently spherical.¹⁴ These cocci were in most cases packed in the protoplasm of the lymphoid and epithelioid cells.¹⁵ In some cases after inoculation from excised papules the plates remained sterile, although an examination of the sections revealed a large accumulation of the cocci in question, while in the hanging drop the above-mentioned corpuscles were always observed in large numbers.

p. 934

At the end of 1897 we began to employ for fixation Zenker's fluid, the composition of which is as follows:—Aq. destillatae 100·0, corrosive sublimate 5·0, potassium bichromate 2·5, sodium sulphate 1·0, acetic acid 5·0.

A freshly excised piece was dropped into this fluid and left there for 12 to 24 hours, after which it was washed for 24 hours in water and then transferred to 60 to 70 per cent. alcohol, absolute alcohol, absolute alcohol + ether, and embedded in celloidin.

After fixation with this fluid we succeeded in discovering in sections masses of corpuscles of the same size and shape as we had observed in the hanging drop.

The younger the papule of Sart sore the greater the number of these corpuscles; the older the papule, or if in the period of ulceration, the fewer these corpuscles; and finally, in old papules with extensive ulceration or in those treated by cauterization, we found them with difficulty and even then in an altered state.

The fresh papule presents the following picture: these corpuscles are absent in the epidermoid and epithelial layers, and are rare in the papillae; the parasites, in most cases enclosed within cells, only make their appearance where the infiltration rises from the deeper layers of the skin to the papillae; the parasites are most numerous in the deeper parts where the accumulation of granulation cells is the greatest. The cells are literally packed with them to such an extent that the limits of the individual parasites cannot be seen, and they appear as one continuous mass in which only their nuclei, stained deeply with Loeffler's solution, are distinctly visible. This is the reason why the earlier preparations produced the impression that these accumulations consisted of cocci. However, deeper down, towards the subcutaneous connective tissue, the accumulations of parasites become less abundant and it is here that they can be observed individually. They proved to be mostly round corpuscles (though some are

p. 936

¹⁴[When the nuclei only of the parasites are visible, an appearance of masses of cocci is produced. However, as will be seen below, the author was fully aware of the true nature of these "cocci."—C.A.H.]

¹⁵[This is the first correct interpretation of the nature of the parasitized host-cells.—C.A.H.]

oval and spindle shaped) with a very faintly stained protoplasm and a sharply stained nucleus situated at the periphery. This nucleus is either round or elongated in shape, while sickle-shaped nuclei are also not uncommon.

As mentioned, these parasites are in most cases situated within cells, the nucleus [of which] is shifted to the periphery, stains badly and is shrivelled, or sometimes destroyed, a cluster of parasites being seen in place of the cell. Accumulations of parasites also occur outside the cells. In such cases there are encountered spheres filled with round corpuscles with a feebly stained protoplasm and a nucleus at the periphery.

Still deeper, where there is no infiltration with the lymphoid elements, in the fissures between bundles of connective tissue and in the perivascular spaces, there can be seen rows and small clumps of the same parasitic cellular structures.

The size of the parasites is in most cases about 1μ , sometimes larger, but rarely smaller. Their nuclei vary in dimensions; sometimes they occupy a considerable part of the whole body, and not infrequently there can be seen a fine process running from the nucleus to the opposite side of the body, the process bearing a small globular thickening.¹⁶

On examining a papule, in which a small ulceration covered with a crust has already been formed, it is seen that the cellular infiltration, having reached the surface of the epithelial layer, has destroyed it and spread over the surface. The infiltration penetrates into the depth and spreads widely, while the parasites together with the granulation elements break their way outwards, though they are considerably less numerous on the surface than in the deeper parts.

On the other hand, the accumulations of lymphoid elements scattered in the subcutaneous connective tissue also contain smaller numbers of the parasites.

Amongst the accumulations of blood found at the bottom of the ulcer are seen considerable numbers of parasites which are occasionally situated within the red blood corpuscles.¹⁷

p. 937 Several times, on examining the juice of the papules in a hanging drop, we have observed the parasites inside the red blood corpuscles, the parasite changing its position and shape. In sections the greatest accumulation of parasites occurs around the vessels where, as already stated, the infiltration is also greatest.

The oldest papule examined by us was about 1 year old. This case had been treated by repeated applications of tincture of iodine. In this instance most of the granulation tissue had passed into the connective tissue and only small accumulations of lymphoid elements were encountered in different parts of the section. The parasites could be detected with difficulty and had undergone alterations: they stained uniformly and most of them had bud-like outgrowths.

¹⁶[This description evidently refers to the whole parasite in which the nucleus and elongated kinetoplast ("process") were seen.—C.A.H.]

¹⁷[Misinterpretation of superimposed position of the parasites. The same error was committed by a number of authors in the case of *Leishmania donovani* (LAVERAN, 1903; LAVERAN & MESNIL, 1903; LEISHMAN, 1903).—C.A.H.]



Рис. 1. Разрѣзъ изъ 2-хъ недѣльной папулы при увелич. 37; более темныя мѣста указываютъ мѣста скопленія грануляціонныхъ элементовъ.



Рис. 2. Тотъ же препаратъ при увеличеніи 1:500 (Масл. сѣст.); въ центрѣ разрѣзъ кисты, наполненной чуждыми.

FACSIMILE OF PAGE 935 IN BOROVSKY'S MEMOIR.

Legend to Figures.

(Translated from the Russian.)

FIG. 1.—Section from papule 2 weeks old, at a magnification $\times 37$: the darker places indicate the areas of accumulation of granulation elements.

FIG. 2.—The same preparation at a magnification $\times 1,500$ (oil immersion): in the centre is a section of a cyst filled with parasites.

[As in the original article, the arrangement of the description is reversed, Fig. 1 (top) bearing the legend of Fig. 2 (bottom), and vice-versa.—C.A.H.]

Что касается нашего изслѣдованія, то данныя, полученные нами, слѣдующія:

1) Въ сокѣ папуль и не воспаленныхъ, еще не старыхъ язвахъ всегда находятся одноклѣточные организмы, которые, повидимому, должны быть отнесены къ классу «protozoa».

2) При посѣвахъ сока язвъ вырастаютъ различнаго вида бактеріи и то въ небольшомъ количествѣ, а иногда посѣвы остаются безплодными.

3) Присутствіе въ мазкахъ и срѣзахъ изъ папуль множества тѣхъ же организмовъ, какіе наблюдаются и въ висячей каплѣ.

4) Обнаруживается масса «protozoa» въ раннемъ періодѣ развитія язвы и уменьшеніе и даже полное исчезновеніе въ очень старыхъ язвахъ; отсутствіе въ то же время какихъ либо дробянокъ въ ранней степени развитія язвы и увеличеніе ихъ количества въ старыхъ язвахъ, изъязвленныхъ, которыя, какъ это отмѣчено всѣми наблюдателями, приближаются къ простымъ язвамъ.

На основаніи всѣхъ этихъ данныхъ мы приходимъ къ заключенію, что сартовская язва вызывается не видомъ какихъ-либо дробянокъ, а организмами болѣе высшаго порядка, — protozoa.

FACSIMILE OF PART OF PAGE 939 IN BOROVSKY'S MEMOIR.

General conclusions, corresponding to pp. 88-89 of the Translation.

To the above it may be added that no schizomycetes could be detected in the non-ulcerating papules by staining.

The parasites described by us stain with Loeffler's solution, the sections being kept in the stain from 2 to 24 hours. Good staining can also be obtained with a saturated aqueous solution of safranin, but the parasites do not stain by Gram's method. We also tried to stain sections by Romanowsky's method (a mixture of eosin and methylene blue) and by the method of Sanfelice, as recommended by the latter for blastomycetes, but though they stained the staining was not sharp. The best method, therefore, is to stain with Loeffler's methylene blue solution followed by rinsing in water and decolorizing in alcohol, but the differentiation should not be carried too far: the same refers to the staining with saturated aqueous solution of safranin.

We failed to obtain cultures of the structures described: inoculations were made into the fluid obtained by puncture of a hydrocele, on agar-agar mixed with ascitic fluid, and in sterile grape juice.

Owing to the peripheral position of the nucleus and to the presence of processes like flagella,¹⁸ we are inclined to refer the parasites described by us to the class of protozoa. Their multiplication apparently takes place both by means of direct division and by budding. We have observed corpuscles in which a short round outgrowth or bud is formed on the periphery, therefore multiplication by budding takes place,¹⁹ though round corpuscles in which a fine process with a thickening at the end is given off from the nucleus occurred more frequently.²⁰ There also occurred corpuscles with two nuclei situated at opposite ends of the body. As the result of slow multiplication there may thus be produced several separate corpuscles enclosed in a common membrane, as was observed by us²¹; whereas in the course of rapid multiplication the division of the nucleus

p. 938

¹⁸[*Vide infra*: footnote 20.]

¹⁹[It is not improbable that the budding forms represent some yeast-like organism which may be present in ulcerating sores and bear some resemblance to Leishman-Donovan bodies when stained (cf. WENYON, 1926, p. 428). The latter interpretation receives support from the fact that a yeast was actually cultivated by the author from sores (cf. p. 88).—C.A.H.]

²⁰[The presence of a "process" in the parasite is mentioned four times in the text (cf. footnotes: 8, p. 84; 16, p. 86; 18, *supra*). According to BOROVSKY, it arises from the nucleus, runs to the opposite side of the body and is provided with a "globular thickening" at the end (there is no indication as to whether it is at the proximal or distal end of the "process"). It is obvious that BOROVSKY must have seen the kinetoplast, either alone or together with the rhizoplast. In the former case the whole "process" would be equivalent to the kinetoplast, in the latter case the "globular thickening" alone would represent this structure, the "process" itself being the rhizoplast. BOROVSKY himself likened the "process" to a "flagellum," but the indications in the text suggesting that in some cases he must have seen only the nucleus of the parasite with the attached "process," coupled with the fact that the kinetoplast always stains deeply and is, therefore, more commonly seen in preparations of the Leishman-Donovan bodies than the rhizoplast, are strong arguments in favour of regarding BOROVSKY's "process" as the kinetoplast. This is the view held by PAWLOWSKY (1927, 1931); and Dr. C. M. WENYON, whom I have consulted on this matter, is of the same opinion.—C.A.H.]

²¹[A condition interpreted by some authors as multiple division.—C.A.H.]

is followed by fission of the protoplasm and separate individuals are produced. It is difficult, of course, to form an exact idea of the method of multiplication from a dead preparation, and not from a pure culture, therefore the account given above represents a personal impression.

In old Sart sores the parasites described are very scanty and they are, moreover, modified—thus there occur round corpuscles similar to those described above in size, but either uniformly stained or in the form of a transparent vesicle only the outline of which is visible. Even when those with nuclei are encountered, the nucleus is considerably smaller than usual and not so deeply stained as in the case of preparations from young papules.

In addition to what has been said above, it must be stated that, up to the present, inoculations from the Sart sores examined were made in Petri dishes and colonies were obtained of staphylococci (most frequently) and sarcinae; moreover, in three cases there developed very minute oval cocci which did not liquefy gelatin and, when examined in the living condition, were mostly arranged in pairs, in the form of diplococci; in one case there appeared in a Petri dish with agar-agar five colonies of microc.[occus] tetragenus; and in another case there developed amongst other colonies pink yeasts, while in two cases the plates remained sterile. The total number of cases examined by us exceeded twenty, nine of which were still in the form of papules.

Of course, we cannot yet extend the results obtained from the investigation of Sart sore to other similar diseases of the skin, such as Pendeh sore, Aleppo boil, [bouton de] Biskra, Elisabethpol "godovik"²², etc., but would suggest the desirability of verifying their nature from the point of view put forward by us. The desirability of this verification is based on the following facts. In his study of Pendeh sore, RAPTSCHESKY makes the following statement: "in spite of repeated investigations, the result of bacterioscopic examinations of the 'lymphangitic' nodules²³ in cases of Pendeh sore remained negative. It was impossible to detect any microorganisms in the juice mixed with blood obtained from incised nodules, either microscopically or by means of cultures."

However, in another place RAPTSCHESKY mentions that under the influence of irritation such a "lymphangitic" nodule may suppurate, open and then heal, like an ordinary abscess; and, further, that these complications in the form of lymphangitis occur in the case of sores which are contaminated or irritated, and in which there is a retention of pus under the crust. If that is the case, why are there no microbes in the "lymphangitic" nodules? However that may be, it is impossible to decide anything *a priori*.

As regards our own investigation, the data obtained by us are as follows:—

(1) In the juice of papules and in sores which are not yet old and have not ulcerated, there are always present unicellular organisms which should apparently be referred to the class "protozoa."

²²[Cf. Footnote 6, on p. 82.]

²³[These are evidently the lymph nodes affected by lymphangitis.—C.A.H.]

(2) In cultures of the juice from sores there grow various kinds of bacteria, though in small numbers, but sometimes the cultures remain sterile.

(3) In smears and sections of papules there are present large numbers of the same organisms which are observed in the hanging drop.

(4) Masses of "protozoa" are encountered in the early period of development of the sore, diminishing and even disappearing completely in very old sores. At the same time bacteria of any kind are absent in the early stages of development of the sore, but they occur in increasing numbers in old ulcerating sores, which, as has been noted by most observers, approximate to ordinary ulcers.

From all these data we arrive at the conclusion that Sart sore is not caused by any kind of bacteria, but by organisms of a higher order, *viz.* protozoa.

As regards the method of infection, we are inclined to think that the infection does not penetrate into the skin directly, but is conveyed either from the intestinal tract or from the respiratory apparatus through the blood. p. 940

The fact that exposed parts of the body are affected by preference can be explained by the greater susceptibility of these parts to traumata and to the appearance of minute capillary haemorrhages in which the accidentally transferred parasites find a suitable material [= *medium*] for development. Owing to the low toxicity of the products of metabolism of these parasites the phagocytes overcome them with comparative ease, and although many of the phagocytes perish, they appear in ever increasing numbers and finally destroy the parasites. That protozoa can find their way into the respiratory tracts has been proved experimentally. Thus, GRASSI and FELETTI demonstrated the presence of an extremely minute amoeba in the nasal cavities of pigeons which remained for two nights in a marshy locality at an altitude of 2 metres above the level of the ground, while 9 days later the same amoebae were found in the blood of the pigeons (LAVERAN et BLANCHARD, *Hématozoaires du Paludisme*). Infection with marsh fevers also takes place through the respiratory tract. Infection through the intestinal tract is possible through water and, it may be, through contaminated food.

As regards water used for washing and bathing, the transmission of infection through this medium is very doubtful, since, in spite of the fact that during the summer heat the entire Russian population of Tashkent bathes in "aryk" water²⁴, cases of this disease are very rare in summer. According to our observations, cases occur more frequently during the winter and spring months of the year. The last circumstance also shows that the rôle of dust in the spread of the disease is insignificant (if indeed it serves as a vector of the infection at all), for during the said time of the year the rainfall in this locality is very heavy.

TREATMENT.

In Tashkent the most commonly used remedy for the treatment of Sart sore is pure lactic acid, which is employed either in an ointment or in a layer of p. 941

²⁴"Aryki" [*pl.*] are shallow canals by which water is conveyed for the irrigation of gardens, kitchen-gardens and fields [*in Turkestan*].

cotton wool impregnated with it and applied to the sore, where it is left for 24 hours. The latter method is more reliable; when it is used the healthy skin around the sore is covered with collodion or an adhesive plaster. After 24 hours the dressing is removed and in place of the previous infiltration a scab is formed under which is a clean ulcerated surface, which is usually treated as an ordinary ulcer.

When the ulcer is cauterized successfully in this manner it heals in the course of 2 to 4 weeks. We have also applied the sublimate ointment recommended by Dr. TEKUTIEV with satisfactory results.

However, in some cases the infiltration re-appeared after cauterization and subsequent cicatrization; in these cases we scraped it thoroughly with a sharp spoon. Scraping was also practised in cases where the eyelids were affected and cauterization could not be employed. A thorough scraping was always followed by healing.

When the papules were excised right down to the subcutaneous connective tissue, we inserted a suture which in most cases resulted in complete healing *per primam intentionem*, though sometimes under the cicatrices a fresh lesion would occur, necessitating either cauterization or scraping.

APPENDIX III.

K. SHULGIN (1902): ON THE TRANSMISSION OF ORIENTAL SORE.

It has already been mentioned (p. 71) that K. SHULGIN, who was BOROVSKY's contemporary at the Tashkent Military Hospital, fully confirmed his colleague's observations on the aetiology of oriental sore. However, SHULGIN's real claim for a place in the history of tropical medicine rests on the views he expressed regarding the transmission of this disease, for he was actually the first to suggest, in 1902, that the vector was a blood-sucking insect. The part played by SHULGIN in enunciating this hypothesis is practically unknown to anyone, either in his own country or outside it. One of the reasons for this is probably the fact that the journal in which SHULGIN's paper was published is just as inaccessible as the one in which BOROVSKY's memoir appeared.

The only reference to SHULGIN's observations which I have been able to discover is a statement occurring in LAVERAN's monograph that "Shulgin croyait que les moustiques étaient les agents de transmission du bouton d'Orient" (LAVERAN, 1917, p. 437*).

It is not indicated, however, that this was actually the first suggestion of the rôle of blood-sucking insects in the transmission of this disease. On the contrary, the preceding paragraph—according to which "dès 1875, SÉRIZIAT déclarait avoir vu des boutons de Biskra ayant incontestablement pour origine des piqûres de moustiques" (*loc. cit.*, p. 437)—might be construed as establishing the priority of SÉRIZIAT, but from an extract of this author's writings appearing

*LAVERAN, A. (1917). *Leishmanioses*. (Paris: Masson et Cie.)

elsewhere in the monograph (*loc. cit.*, pp. 429-430) it is obvious that SÉRIZIAT merely asserted that the slightest lesion in the skin may serve as the starting point of oriental sore, and that he himself had seen sores originating at the site of a mosquito-bite. He did not, therefore, imply that the disease was disseminated by the mosquito, but that this insect was one of the agents, including mechanical ones, capable of impairing the intactness of the skin and thereby exposing it to infection.

SHULGIN's paper—"The question of the aetiology of Pendeh sore"—was written in Russian and published in the journal *Russkij Vrač* [= The Russian Physician], 1902, Nos. 32 and 33, pp. 1150 and 1180. These issues are unobtainable in this country, and I am indebted to the late Prof. G. W. EPSTEIN, of Moscow, for a typewritten *verbatim* copy of SHULGIN's article, from which I have translated the most interesting passages relating to the transmission of oriental sore.

After discussing the views of other Russian observers, who believed that the causative organism was found in water, or in the soil, and was disseminated by dust through the air, SHULGIN proceeds as follows:—

"However, I am inclined to consider that the mode of penetration of the infective agent into the body is the same as that recognized at present for marsh fever, *i.e.*, that it has an intermediate host—a mosquito or some other nocturnal biting insect."

The author then goes on to substantiate his contention:—

"In eight cases I succeeded in observing the very earliest phase of the disease, the primary papule, [at a period] when it was even impossible to identify it with certainty, but from which a typical Pendeh sore developed later. It then appeared in the form of a reddish, raised, compact spot, as large as a lentil. In the middle there was always a darker point, similar to that in the centre of a mosquito or flea bite. Intelligent persons in whom I observed such primary papules testified that they had actually been bitten in these places by something on a previous evening. . . . Moreover, on the assumption that the infection is spread by insects, it is easy to explain why the sore appears only during a certain period of the year. In all the localities where the disease is endemic cases are observed at the end of summer and at the beginning of autumn exclusively. . . . This can be fully accounted for on the basis of the mosquito theory, for mosquitos appear in large numbers in July. The time between their appearance and the occurrence of the first cases of the disease is taken up by the infection [of the insects], the development of the microorganism in them, its inoculation [to man], and the incubation period. In October the mosquitos disappear and no fresh cases occur while the old sores sometimes persist for 2 years. . . ."

SHULGIN also quotes the following observation in support of his views: In a certain locality of Turkestan the officers and men of the garrison shared the same barracks, but cases of oriental sore occurred among the privates exclusively. According to the author, this was due to the fact that only the officers slept under mosquito-nets and were, therefore, protected from the bites of the insects.

Lastly, SHULGIN notes that the sores appear most frequently on those parts of the body which are covered in the daytime, but may be exposed in the night (arms, legs).

In conclusion, the author makes the following statement : " As I said at the beginning, the insect transmitting the infection must be nocturnal, and now I more definitely attribute it to the mosquitos."

In the foregoing passages the case is presented in such a lucid manner and the arguments brought forward are so convincing that no special comments are required. It will be noted how near SHULGIN was to the correct solution of the nature of the vector of oriental sore, for all the observations and arguments adduced by him in support of his hypothesis regarding the transmission of the infection by mosquitos are equally applicable to the sandflies, which, in Turkestan, usually make their appearance in the middle of June and disappear towards the beginning of October, while the similarity of the feeding habits of both these groups of insects is well known.

